Direct Dichlorovinylation of Nitriles with Trichloroethylene Under Phase-Transfer Catalysis Conditions

Andrzej Jończyk,* Agnieszka H. Gierczak

Warsaw University of Technology, Faculty of Chemistry, Koszykowa 75, P-00662 Warsaw, Poland
Fax +48(22)6282741; E-mail: anjon@ch.pw.edu.pl

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Abstract: Reaction of trichloroethylene with nitriles **1a–k**, carried out in the presence of 50% aqueous sodium hydroxide and tetrabutylammonium hydrogen sulfate as a phase-transfer catalyst, in diethyl ether at 5–10 °C affords dichlorovinyl derivatives **2a–k** in good yields. Deprotection of the latent carbonyl group in aminonitrile **1f** results in the formation of dichlorovinyl ketone **5**.

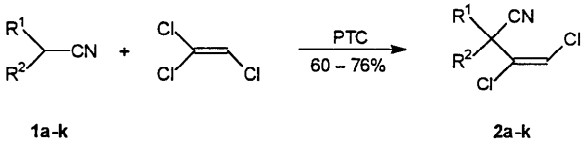
Key words: phase-transfer catalysis (PTC), nitriles, trichloroethylene, dichloroacetylene, dichlorovinylation reaction

Trichloroethylene smoothly eliminates hydrogen chloride on treatment with a base to generate dichloroacetylene, which can be isolated or, in turn, added to nucleophiles with formation of 1,2-dichlorovinyl derivatives and/or other products.[1] A particularly convenient method for the preparation of dichloroacetylene consists of the reaction of trichloroethylene with a 50% aqueous sodium hydroxide solution and a quaternary ammonium salt[2] or DMSO[3] as a catalyst in diethyl ether [phase-transfer catalysis (PTC) conditions[4,5]]. Diethyl ether forms a fairly stable, distillable complex with dichloroacetylene which otherwise explodes in air. PTC reactions of trichloroethylene with secondary aliphatic or cyclic amines give *N*,*N*,*N'*,*N'*-tetraalkylglycinamides,[6] while with some heterocycles (imidazole, pyrazole, carbazole), *N*-dichlorovinyl-substituted products are formed.[7] Competitive reactions of trichloroethylene with mixtures of carbazole and primary or secondary amines lead to the formation of *N*-dichlorovinylcarbazole as the main product.[7] Phenols or selenophenol react with trichloroethylene under PTC conditions to afford aryl 1,2-dichlorovinyl ethers[8] and 1,2-dichlorovinyl phenyl selenide,[9] respectively.

To the best of our knowledge, reactions of carbanions generated under PTC conditions with trichloroethylene or dichloroacetylene have not been reported, yet such processes can be realized by means of other base–solvent systems. Thus, tertiary enolates generated from esters, and cyclic and acyclic ketones give either dichlorovinyl- and chloroethynyl-substituted derivatives, depending on the kind of substrate (trichloroethylene or dichloroacetylene) and the base used (NaH, LDA or LHMDS).[10] If secondary enolates are used (e.g. ethyl malonate anion[10]), more complex structures are formed.

We wish to report here that reaction of nitriles **1a–k** with trichloroethylene under PTC conditions is a convenient method for the preparation of 1,2-dichlorovinyl derivatives **2a–k** (Scheme 1).

Preliminary experiments which consisted of stirring **1a**, excess trichloroethylene and tetrabutylammonium hydrogen sulfate (TBAHS) as a catalyst (15 mol%) in diethyl ether at ca. 35 °C resulted in the formation of **2a** in a yield of ca. 30% together with a significant amount of acetophenone (the oxidation product of **1a**), and tarry materials. When the same reaction was carried out at 5–10 °C, **2a** was isolated in 66% yield. A similar result was obtained with DMSO, while the use of benzyltriethylammonium chloride (TEBAC) as a catalyst afforded **2a** in lower yield, and significant amounts of impurities. Taking into account the above results, and the increased tendency of nitriles to undergo oxidation with oxygen in DMSO[11,12] (also, see below), the reactions of all CH acids **1** with trichloroethylene were carried out at 5–10 °C with TBAHS as catalyst; under these conditions dichlorovinyl derivatives **2** were obtained in 60–76% yield (Tables 1 and 2).



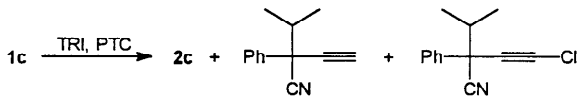
1a-k **2a-k**

1,2	a	b	c	d	e	f
R^1	Ph	Ph	Ph	Ph	Ph	Ph
R^2	Me	Et	*i*-Pr	$PhCH_2$	$Me_2N(CH_2)_2$	Me_2N

1,2	g	h	i	j	k
R^1	Ph	Ph	Ph	Ph	Me
R^2	$O(CH_2CH_2)_2N$	MeO	*i*-PrO	$CH_2=CHCH_2O$	PhS

Scheme 1

The effect of temperature and the kind of catalyst on the reaction course was particularly evident in the case of the sterically crowded nitrile **1c** (Scheme 2, Table 3).



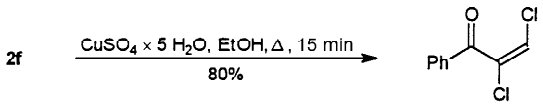
3 **4**

TRI = Trichloroethylene
Scheme 2

The attempted isolation of pure products **3** and **4** from these mixtures by column chromatography failed, therefore they were identified by GC/MS, by comparison with independently synthesized samples (compound **3**[13]) or by chemical methods (compound **4**). If the product mixture from the reaction listed under entry 4 in Table 3 was

stirred with Cu powder/acetic acid/THF (the reagent used for the transformation of the chloroethynyl into the ethynyl group[10]), the amount of **3** increased at the expense of **4** which at the end had been totally consumed.

Dichlorovinylation of α-amino nitriles **1f,g** has to be carried out in the presence of TBAHS, because they are quantitatively oxidized to *N*,*N*-disubstituted benzamides when DMSO is used. Such an oxidation process is known.[12] Nitriles **2f–k**, α-substituted with a heteroatom, possess a masked carbonyl group and are potential sources of dichlorovinyl-substituted ketones. Indeed, refluxing of **2f** with $CuSO_4 \cdot 5H_2O$ in ethanol afforded the expected ketone **5** in high yield (Scheme 3).



Scheme 3

Table 1. Dichlorovinyl Derivatives **2** Prepared

Product[a]	R^1	R^2	Reaction Time (h)	Yield (%)	bp (°C/Torr) or mp (°C)
2a	Ph	Me	3.5	66[b]	75–76/0.04
2b	Ph	Et	4.0	67	110/10
2c	Ph	*i*-Pr	6.5	75[b]	98–100/0.02
2d	Ph	$PhCH_2$	5.0	76	86–88[c]
2e	Ph	$Me_2N(CH_2)_2$	5.0	70	74–76[c]
2f	Ph	Me_2N	4.0	60	113–115[c]
2g	Ph	$O(CH_2CH_2)_2N$	4.5	69	138–141[c]
2h	Ph	MeO	4.0	65	108/0.5
2i	Ph	*i*-PrO	4.5	65	105/0.5
2j	Ph	CH_2=$CHCH_2O$	4.0	61	145–148/11
2k	Me	PhS	5.0	67	112–114/0.2

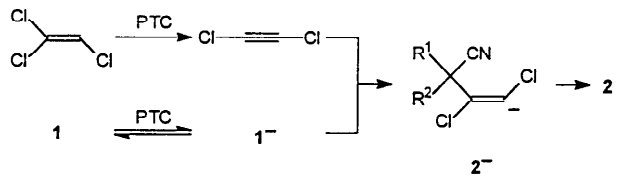
[a] Purity ≥ 98% (GC). All compounds gave satisfactory elemental analyses: C ± 0.19, H ± 0.14, N ± 0.21, Cl ± 0.38.
[b] Distilled products **2a** and **2c** (purity 88% and 83%, respectively) were purified by column chromatography (Merck silica gel 60, eluent: hexane/EtOAc, 4:1).
[c] Crystallized from hexane.

Table 3. Reaction of **1c** with Trichloroethylene Under Different Conditions

Entry	Catalyst	Solvent	Temp (°C)	Time (h)	Products,[a] Yield (%)		
					2c	**3**	**4**
1	TBAHS	Et_2O	5–10	6.5	78	2	12
2	TBAHS	Et_2O	ca. 35	5	24	24	46
3	TBAHS	Pr_2O	ca. 50	4.5	10	33	31
4	DMSO	Pr_2O	ca. 50	4.5	37	5	34

[a] Determined by GC of distilled mixtures.

The products **2** are formed via *trans*-addition of carbanions $\mathbf{1}^-$ to dichloroacetylene and protonation of the thus generated highly basic vinyl anions $\mathbf{2}^-$ (Scheme 4).



Scheme 4

Quite similar results from the reaction of **1b** with preformed dichloroacetylene, or with trichloroethylene, fully support this mechanistic pathway. Addition of nucleophiles (particularly carbanions) to carbon–carbon triple bonds is postulated to occur via a *trans*-mode.[14,15] Therefore, in our case, *E*-dichlorovinyl derivatives **2** are formed. Such an arrangement of chlorine and hydrogen atoms disfavours the base-promoted elimination of hydrogen chloride,[14] and arrests the reaction with the formation of **2**. The product **4** (Scheme 2) may be formed either via a *cis*-addition of $\mathbf{1c}^-$ to dichloroacetylene with subsequent elimination of hydrogen chloride, via addition of $\mathbf{1c}^-$ to trichloroethylene followed by elimination of two equivalents of hydrogen chloride, or via halogenophilic reaction of $\mathbf{1c}^-$ with dichloroacetylene. All these mechanisms have been identified in reactions of nucleophiles with trichloro-

Table 2. ^{1}H NMR Data of Products **2**

Product	^{1}H NMR ($CDCl_3$/TMS) δ, *J* (Hz)
2a	2.01 (s, 3H, CH_3), 6.54 (s, 1H, =CH), 7.37–7.48 (m, 5H, ArH)
2b	1.06 (t, *J* = 7.3, 3H, CH_3), 2.37 (qq_{AB}, ^3J = 7.3, J_{AB} = 13.7, 2H, CH_2), 6.52 (s, 1H, =CH), 7.36–7.48 (m, 5H, ArH)
2c	0.84 (d, *J* = 6.8, 3H, CH_3), 1.33 (d, *J* = 6.4, 3H, CH_3), 2.91–3.04 (m, 1H, CH), 6.42 (s, 1H, =CH), 7.36–7.40 (m, 3H, ArH), 7.55–7.60 (m, 2H, ArH)
2d	3.25 (s, 2H, CH_2), 6.57 (s, 1H, =CH), 6.90–6.94 (m, 2H, ArH), 7.18–7.21 (m, 3H, ArH), 7.31–7.32 (m, 5H, ArH)
2e	2.23 (s, 6H, 2 × CH_3), 2.29–2.72 (m, 4H, 2 × CH_2), 6.50 (s, 1H, =CH), 7.25–7.47 (m, 5H, ArH)
2f	2.30 (s, 6H, 2 × CH_3), 6.33 (s, 1H, =CH), 7.37–7.41 (m, 3H, ArH), 7.74–7.77 (m, 2H, ArH)
2g	2.57–2.64 [m, 4H, $N(CH_2)_2$], 3.78–3.83 [m, 4H, $O(CH_2)_2$], 6.39 (s, 1H, =CH), 7.36–7.44 (m, 3H, ArH), 7.75–7.80 (m, 2H, ArH)
2h	3.56 (s, 3H, CH_3), 6.58 (s, 1H, =CH), 7.42–7.45 (m, 3H, ArH), 7.62–7.65 (m, 2H, ArH)
2i	1.23 (d, *J* = 5.9, 3H, CH_3), 1.36 (d, *J* = 6.4, 3H, CH_3), 4.08–4.13 (m, 1H, CH), 6.53 (s, 1H, =CH), 7.38–7.41 (m, 3H, ArH), 7.61–7.63 (m, 2H, ArH)
2j	4.20–4.24 (m, 2H, OCH_2), 5.25–5.48 (m, 2H, =CH_2), 5.93–6.07 (m, 1H, =CH), 6.53 (s, 1H, =CH), 7.42–7.45 (m, 3H, ArH), 7.65–7.68 (m, 2H, ArH)
2k	4.02 (s, 3H, CH_3), 5.52 (s, 1H, =CH), 7.16–7.25 (m, 5H, ArH)

ethylene or dichloroacetylene.[10,16] Ethynyl derivative **3** probably results from a halogenophilic reaction of any anion present in the system with **4**.[16]

In summary, we have presented an attractive method for the preparation of dichlorovinyl-substituted nitriles **2**. Furthermore, a simple cleavage of α-heteroatom-substituted nitriles **2** opens up a convenient route for the synthesis of aryl dichlorovinyl ketones.

Melting points (capillary tube) and boiling points are uncorrected. ^{1}H NMR spectra were recorded on a Varian Gemini 200 spectrometer in $CDCl_3$. GC/MS were recorded on a Hewlett–Packard 5972A-MSD apparatus. GC analyses were carried out on a Hewlett–Packard 5890 apparatus equipped with a glass capillary column (30 m) and FID. The following nitriles were prepared according to literature procedures: **1a,b**,[17] **1c–e**,[18] **1f**,[19] **1g**,[20] **1h–j**,[21] **1k**[22] and **3**.[13] Other reagents and all solvents are commercially available.

Caution: Fumes of dichloroacetylene may explode on contact with air.

Dichlorovinyl-Substituted Nitriles 2; General Procedure:
A stirred mixture of nitrile **1** (20 mmol), 50% aq NaOH (6.0 g, 4.0 mL, 75 mmol) and TBAHS (1.0 g, 3.0 mmol) was cooled to 5–10 °C. Then, a solution of trichloroethylene (3.15 g, 2.2 mL, 24 mmol) in Et_2O (1.9 g, 2.7 mL, 26 mmol) was added at 5–10 °C over 30 min. The mixture was stirred at 5–10 °C for the time indicated in Table 1, diluted with H_2O (20 mL), and the phases were separated. The H_2O phase was extracted with benzene (2 × 10 mL). The combined organic phases were washed with H_2O (2 × 10 mL), dried ($MgSO_4$), and the solvent was evaporated on a rotary evaporator. The residue was distilled in vacuo (**2a–c,h–k**) and additionally purified by column chromatography (**2a**,**c**) or crystallized (**2d–g**) (Tables 1 and 2).

Reaction of Nitrile 1c with Trichloroethylene in DMSO:
A mixture of nitrile **1c** (1.0 g, 6 mmol), 50% aq NaOH (3.0 g, 2.0 mL, 38 mmol) and DMSO (0.05 g, 0.06 mmol) was stirred and heated to ca. 55 °C. To this mixture was added dropwise a solution of trichloroethylene (1.0 g, 0.7 mL, 8 mmol) in dipropyl ether (0.9 g, 1.2 mL, 9 mmol) at 50–55 °C over 20 min. The mixture was stirred at 50–55 °C for 4 h, cooled, diluted with H_2O (15 mL), and the phases were separated. The H_2O phase was extracted with CH_2Cl_2 (2 × 5 mL), and the combined organic phases were washed with H_2O (2 × 7 mL) and dried ($MgSO_4$). The solvent was evaporated and the residue was distilled (bp 90–110 °C/0.2 Torr, 1.3 g). GC analysis showed the presence of **2c** (46%), **3** (3%) and **4** (36%).The distillate was also analysed by GC/MS.
GC/MS (EI): *m*/*z* (relative intensity,%) = **2c**, 253 (M^+, 11); **3**, 183 (M^+, 1); **4**, 217 (M^+, 1).
The above obtained mixture (0.10 g) and Cu powder (0.05 g, 0.83 mmol) were suspended in THF (10 mL). Then AcOH (1 mL) was added, the mixture heated for 2 h at 70 °C, cooled, diluted with H_2O and extracted with CH_2Cl_2 (3 × 5 mL). The organic extracts were dried ($MgSO_4$) and the solvent was evaporated. The residue (0.095 g) was analysed by GC to show **2c** (62%), **3** (30%) and **4** (0.5%).

1,2-Dichlorovinyl Phenyl Ketone (5):
A mixture of the amino nitrile **2f** (1.50 g, 5.9 mmol), $CuSO_4$•$5H_2O$ (1.50 g, 5.9 mmol) and EtOH (5 mL) was refluxed for 15 min and cooled. To this mixture was added benzene (5 mL) and the phases were separated. The H_2O phase was extracted with benzene (2 × 5 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by column chromatography (Merck silica gel 60, eluent: hexane) to give the ketone **5** (0.95 g, 80%); (Lit.[23] bp 160–161 °C/38 Torr).
^{1}H NMR: δ = 6.39 (s, 1 H, =CH), 7.26–7.44 (m, 3 H, ArH), 7.75–7.82 (m, 2 H, ArH).
Anal. $C_9H_6Cl_2O$ (201.1): calcd C, 53.75; H, 3.00; Cl, 35.26; found C, 53.60; H, 3.06; Cl, 34.96.

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